STUDIES ON \textit{as}-TRIAZINE DERIVATIVES. X.\textsuperscript{1} ADDITION REACTION OF PHENYL-MAGNESIUM BROMIDE WITH 1,2,4-TRIAZINES

Shoetsu Konno, Mataichi Sagi, Nobuko Yoshida, and Hiroshi Yamanaka* 
Pharmaceutical Institute, Tohoku University 
Aobayama, Sendai 980, Japan

Abstract ——— The reaction of 1,2,4-triazine with phenyl-magnesium bromide was investigated. Every position of 3, 5, and 6 in a 1,2,4-triazine ring is active in the addition reaction of Grignard reagents. Since 5-phenyl-1,2,4-triazine, 5,6-diphenyl-1,2,4-triazine, and 3,5,6-triaryl-1,2,4-triazine were obtained subsequently, it was confirmed that the most active position was position 5 and the least active one was position 3.

In order to estimate the relative reactivity of position 3, 5, and 6 in a 1,2,4-triazine (\textit{as}-triazine) ring, the reaction of unsubstituted \textit{as}-triazine (1) with phenylmagnesium bromide was investigated.

Although the reaction at room temperature gave resinous materials, the reaction of 1 with three mole equivalent amount of phenylmagnesium bromide at \(-50^\circ\text{C}\) proceeded smoothly, and 5-phenyl-\textit{as}-triazine (3), mp 103-105\textdegree\text{C}, was isolated (45\% from 1) exclusively by alkaline ferric cyanide oxidation of the crude dihydro-intermediate (2).\textsuperscript{2} The spectral data and melting point of the product (3) were identical with those of an authentic specimen prepared by a reported method.\textsuperscript{3} Then the reaction of 3 with phenylmagnesium bromide was investigated. In this case, the reaction proceeded smoothly in an ether medium at room temperature, and 1,6-dihydro-5,6-diphenyl-\textit{as}-triazine (4) mp 159-160\textdegree\text{C}, was obtained in good yield. The sodium borohydride reduction of 4 followed by potassium ferric cyanide oxidation gave 5,6-diphenyl-\textit{as}-triazine (5), mp 114-116\textdegree\text{C}, in 57\% yield from 4, which was identical with an authentic specimen prepared by the reported
In connection with the reaction sequence, the direct oxidation of 4 to 5 failed, although the reason is not clear at present.

Based on these results, it is suggested that in a \textit{a}s-triazine ring system, the most active position for Grignard reaction is position 5 and the least active one is position 3. In the relatively less reactive position, however, Grignard reaction occurs efficiently. Namely, 5,6-diphenyl-as-triazine (5) reacted with \textit{p}-methoxyphenylmagnesium bromide in ether and 3-(\textit{p}-methoxyphenyl)-5,6-diphenyl-as-triazine (6), \textit{mp} 161-162°C (lit.\textsuperscript{4} mp 164°C), was isolated in 53\% yield by the subsequent oxidation of the crude adduct with \textit{N}-chlorosuccinimide in triethylamine. Like in the case of 1, the reaction of 3-methylthio-as-triazine (7) with phenylmagnesium bromide at -50°C gave selectively 2,5-dihydro-3-methylthio-5-phenyl-as-triazine (8),\textsuperscript{5} \textit{mp} 99-103°C in 77\% yield. Potassium ferric cyanide oxidation of 8 under alkaline conditions afforded 3-methylthio-5-phenyl-as-triazine (9), \textit{mp} 97-99°C (lit.\textsuperscript{6} mp 99-100°C), as a sole product (80\%).

\begin{center}
\textbf{Scheme 1}
\end{center}

The compound 9 underwent the addition with phenylmagnesium bromide to give an adduct (10). Although 10 was not purified, like 4, the sodium borohydride treatment...
reduction of the crude adduct (10) followed by potassium permanganate oxidation gave rise to aromatization, and 3-methylthio-5,6-diphenyl-as-triazine (11), mp 120-121°C (lit. mp 121-122.5°C) was obtained. These findings are consistent with those observed on the reaction of 1 with phenylmagnesium bromide.

Typical experiments are as follows: 5-Phenyl-as-triazine (3) ——— To a solution of as-triazine (1) (0.57 g, 0.007 mol) in dry THF (10 ml) was added dropwise a Grignard solution [prepared from Mg (0.34 g, 0.0014 g atom) and bromobenzene (2.29, 0.0014 mol) in dry THF (10 ml)] at -50°C under nitrogen over a period of 10 min and the mixture was stirred for 1.5 h. After the removal of the cool bath, the reaction mixture was stirred for 1.5 h at room temperature. The Grignard complex was decomposed with saturated aq. NH₄Cl and the organic layer was separated. The aq. layer was extracted with ether (20 ml). The organic layer was combined and dried over MgSO₄. After removal of the solvent under reduced pressure, a mixture of K₃Fe(CN)₆ (6.9 g, 0.002 mol), 3 N NaOH (9.3 ml), H₂O (40 ml) and CH₂Cl₂ (30 ml) was added to the residue and vigorously stirred for 12 h at room temperature. The organic layer was separated and dried over MgSO₄. After the solvent was removed, the residue was purified by silica gel column chromatography using hexane-ether (1:1) as an eluent. Recrystallization from hexane gave 0.49 g (45 %, yield from 1) of 5-phenyl-as-triazine (3), mp 103-105°C (lit. mp 103°C) as pale yellow needles. ¹H-Nmr (CCl₄): 7.3-7.8 (3H, m), 7.9-8.4 (2H, m), 9.55 (1H, d, J=2 Hz), 9.66 (1H, d, J=2 Hz).

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REFERENCES AND NOTES


2. The compound 2 was unstable for further purification, so the dihydro-structure of this compound was not determined evidently.


5. The structure of 2,5-dihydro-3-methylthio-5-phenyl-as-triazine obtained by sodium borohydride reduction of 9 had been determined by means of X-ray crystallography (T. Sasaki, M. Minamoto, and K. Harada, *J. Org. Chem.*, 1980, **45**, 4587). Our compound (8) was identical with the authentic specimen prepared by the reported method.


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